REMARKS

In this amendment and response, the specification has been amended to present SEQ ID NOS. at various locations in the specification. In addition, claims have been amended and added as presented in the listing of claims. The amended and new claims are supported by the original disclosure and claims, in particular, the specification, *inter alia*, at page 182, lines 1-10; and pages 183 -187 (Table 10). Accordingly, no new matter has been added by virtue of the new and amended claims.

Applicants request cancellation of the non elected claims without prejudice or disclaimer, and reserve the right to timely file one or more divisional applications covering the subject matter of any and all of the non elected claims.

In the communication dated April 18, 2003, the Examiner subjected the pending claims 1-111 to restriction under 35 U.S.C. §121. The claims were restricted into fifteen (15) groups which are considered by the Examiner to be distinct inventions. The Examiner further restricted the claims to a single sequence.

To provide a complete response to this communication, applicants elect claims of Group I, representing claims 1-20,31-36, 41-49, 56-59, 86-91 and 96-99 (*i.e.* claims drawn to an isolated nucleic acid and varients thereof, and a vector, host cell, pharmaceutical composition, and kit comrpising said nucleic acid) for examination purposes in the subject application. In addition, applicants further elect SEQ ID NO.: 19 with the single polymorphism set forth in SEQ ID NO: 5969 (*i.e.* gene 454.1 as set forth in Table 4 with the G>A mutation as set forth as H 1 in Table 10).

This election is made with traverse. It is believed that since a discrete number of SNP sequences of Table 10 reside within the sequence of Gene 454, (SEQ

ID NO.:19), the Examiner could, without undue burden on his time or searching efforts, search and examine the elected SNP sequence, as well as at least a subset of the SNPs specified in Table 10 that are variants of Gene 454. Such SNPs in particular constitute SEQ ID NOS.: 5955-5984. More particularly, SEQ ID NOS.:5955, 5957 to 5958, 5961 to 5968, 5972, 5974 to 5975, 5977 to 5978, 5980, 5982, and 5984, could be searched and examined, without undue burden on Examiner's time or searching efforts, as these SNPs do not change the encoded amino acid sequence. See MPEP §2434 8th Ed. Rev. No.1. ("Nucleotide seqeunces encoding the same protein are not considered to be independent and distinct and will continue to be examined together.") The SNPs are either in non-coding regions (*i.e.* SEQ ID NOS.:5955, 5957 to 5958, 5962 to 5968, 5972, 5974 to 5975, and 5977 to 5978) or silent mutations (*i.e.* SEQ ID NOS.: 5961, 5980, 5982, and 5984).

It is respectfully submitted that a reasonable search could encompass the variant polynucleotide sequences for gene 454 of Table 10, which are contained in the sequence of SEQ ID NO.:19 with the single polymorphisms set forth in SEQ ID NOS.:5955-5984. The sequences are related, and a search of one would necessarily overlap with a search of the others. Accordingly, it is respectfully submitted that it would not impose a burden on the Examiner to examine at least the presently claimed sequences of Gene 454 in Table 10 in the same group.

It is also respectfully contended that a search for nucleic acid sequences having at least a 95% identity, particularly, a 97%-99% identity, or more particularly, a 99% identity, with the nucleic acid sequence of SEQ ID NO.:19 would uncover any art, if extant, that may be pertinent to the sequences of the SNPs as listed in Table 10 and

recited in the present claims. Accordingly, it is believed that a single and comprehensive search can be readily conducted using the reasonable parameters for identity percentages for polynucleotide sequences as set forth above without an undue burden on the Examiner's time. Thus, a single search with high percent identity parameters is believed to be able to be carried out in which at least the specified subset of polymorphisms set forth in SEQ ID NOS.:5955-5984, or even more particularly, SEQ ID NOS.:5955, 5957 to 5958, 5961 to 5968, 5972, 5974 to 5975, 5977 to 5978, 5980, 5982, and 5984, are searchable together without a serious imposition on the Examiner's task and time.

Because the SNPs listed in Table 10 for Gene 454 comprise combinations, and in particular, haplotypes, which are associated with the asthma phenotype and other related diseases, SNP combinations for Gene 454 should be viewed together in their association with disease. Asthma is a complex disease and as such involves various combinations of SNPs which contribute to the disease.

Also, as particular examples, Example 12 describes eighteen SNP combinations which have p-values < 0.01 in gene 454 in the combined population for the asthma phenotype. *See* page 225. For example, the haplotype consisting of SNP E2 and F-2 had a p-value of 0.001 in the combined population. *Id.* Similarly, four SNP combinations have p-values <0.01 in Gene 454 in the combined population for bronchial hyper-responsiveness. *See* page 226. Thirteen SNP combinations have p-values <0.01 for elevated levels of total IgE and sixteen SNP combinations have p-values < 0.01 for elevated levels of specific IgE. *See* pages 227-228. Because combinations of more than one of the SNPs listed in Table 10 can be linked to the asthma phenotype,

bronchial hyper-responsiveness and/or elvated levels of total or specfic IgE, a search of the art should properly include more than a single SNP, so as not to unduly limit the significance of SNP combinations in applicants' invention to merely a single species. Accordingly, it is respectfully requested that a reasonable search be conducted in which all of the claimed SNPs, which comprise a reasonable number of sequences, are included. Such a request is believed not to place an excessive search burden on the Examiner.

AUTHORIZATION

Should fee(s) additional to those paid herein be necessary for the filing of this response, the Commissioner is hereby authorized to charge any fee(s) which may be deemed assessable in this application to Deposit Account No. **13-4500**, Order No. **2976-4044US1**.

Respectfully submitted,

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